Editorial Commentary

Cerebrovascular Challenges in Diabetic Patients
The Pressure Is on to Maintain Perfusion

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In this edition of Hypertension, Kim et al report that cerebral perfusion is differentially affected by pharmacological blood pressure treatment in hypertensive patients, uncomplicated type II diabetics, and type II diabetics with microvascular complications. Specifically, they reported a progressive decrease in cerebral blood flow after 6 months of antihypertensive medication in diabetics with microvascular complications, whereas cerebral blood flow in hypertensive or uncomplicated diabetics was only marginally reduced by treatment. In addition, the diabetics with microvascular complications demonstrated a blunted cerebral responsiveness to CO₂ but similar middle cerebral artery blood velocity compared with hypertensives and uncomplicated diabetics before treatment for their hypertension. However, it is unknown whether the blunted cerebral vasodilator responses at baseline were caused by the same mechanisms that reduced middle cerebral artery blood velocity after blood pressure treatment.

When the findings of Kim et al are viewed in an epidemiological context, it is interesting to note that, in middle-aged and older humans, obesity, diabetes mellitus, hypertension, and physical inactivity frequently coexist in the same patients. All of these conditions are associated with vascular dysfunction in both large conduit vessels and the microcirculation, and all have emerged as major risk factors for mild cognitive impairment and Alzheimer disease. Furthermore, reduced brain volume associated with any of these conditions may mediate the decline in cognitive function. By contrast, recent evidence suggests that physical activity might be protective against mild cognitive impairment and Alzheimer disease, although the mechanisms are unknown. Extrapolation of the data from Kim et al suggests a potential physiological link between so-called vascular risk factors and cognitive decline in patients with long-standing diabetes mellitus and hypertension.

In this context, a few questions come to mind. First, because diabetes mellitus is associated with macrovascular and microvascular dysfunction, is it possible that high resting blood pressure in complicated diabetes mellitus is a compensatory mechanism to maintain adequate cerebral perfusion? This concept has emerged for other critical organs like the heart and kidneys, but does it also operate in the brain?

Second, does reduced cerebral vasodilator responsiveness to CO₂ mean that cerebral vasodilator responses to increased neural activity will also be blunted? Third, is the reduced cerebral vasodilator response attributed to the effects of hyperglycemia, per se, or does it reflect a more long-term maladaptive response to diabetes mellitus? Fourth, will blunted cerebral vasodilator responses to increased neural activity eventually cause brain atrophy? Finally, will this lead to a vicious cycle of reduced cerebral perfusion, brain atrophy, and lower metabolic demand? In addition, whereas increases in perfusion pressure in the short run might maintain cerebral blood flow, over time they might evoke so-called end organ damage and further deteriorate the inherent ability of the cerebral microvessels to dilate in response to chemical, autoregulatory, or metabolic stimuli. Thus, how do we maintain blood flow in the normal range and enhance local vasodilator responses in the absence of a rise in blood pressure?

In other vascular beds, endurance exercise interventions consistently demonstrate improved macrovascular and/or microvascular function in middle-aged and older adults. These findings clearly provide a rationale for examining the effect of endurance exercise training on cerebral perfusion, particularly in diabetics and/or hypertensive individuals with microvascular complications. The diabetic patients would be further served by the powerful antidiabetic effects of exercise. If endurance exercise training improves microvascular function in middle-aged and older adults, the effect is likely systemic and will, therefore, improve cerebral perfusion. Maintaining or increasing cerebral perfusion (in addition to cerebral responsiveness to CO₂ and autoregulatory mechanisms) is also of critical importance in aging humans who are at risk for both cognitive decline and vascular dysfunction. Cognitive function is closely associated with cerebral blood flow and brain atrophy, and a reduction in either may precipitate the age-related decline in cognitive function. The association between brain volume and blood flow is particularly striking in individuals with either mild cognitive impairment or mild Alzheimer disease. In this context, physical activity has been shown to prevent the age-related decline in cognitive function and may be associated with a greater brain volume. Although Kim et al showed that cognitive function did not change over the 6 months of treatment, longer-term follow-up may be necessary for interventional studies.

In conclusion, the epidemiological evidence clearly shows reduced mortality and incidence of cardiovascular events with blood pressure–lowering medications. However, it is unclear what the impact of this treatment has on long-term cognitive function and how it is physiologically linked to
changes in brain blood flow. Finally, will exercise training in fact triple the reward in hypertensive diabetics by improving their blood pressure, improving glycemic control, and improving brain blood flow?

Disclosures

None.

References

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Hypertension. 2011;57:674-675; originally published online February 28, 2011;
doi: 10.1161/HYPERTENSIONAHA.110.168070

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